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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NUMBER: **10/080,979**
FILING DATE: **February 22, 2002**
FIRST NAMED INVENTOR: **Phillip Dan Cook**
ART UNIT: **1635**
EXAMINER NAME: **Amy Hudson Bowman**
ATTORNEY DOCKET NUMBER: **ISIS-5028**
TITLE: **METHOD OF USING MODIFIED
OLIGONUCLEOTIDES FOR HEPATIC
DELIVERY**

I certify that this communication is being deposited with the United Parcel Service in a box addressed to United States Patent and Trademark Office, Customer Service Window, Mail Stop Amendment, Randolph Building, 401 Dulany Street, Alexandria, VA 22314 on the date shown below:

Dated: 6/1/2005 By: Kemlyn Evans
Kemlyn Evans

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
Under 37 C.F.R. §§ 1.56 and 1.97-98

SIR:

Pursuant to the provisions of 37 C.F.R. §§ 1.56 and 1.97-98, enclosed herewith is PTO Form PTO/SB/08A and PTO/SB/08B listing references for consideration by the Examiner.

The filing of this Information Disclosure Statement shall not be construed as a representation regarding the completeness of the list of references, or that inclusion of a reference in this list is an admission that it is prior art or is pertinent to this application, or that a search has been made, or as an admission that the information listed is, or may be considered to be, material to patentability, or that no other material information exists, and shall not be construed as an admission against interest in any manner.

06/09/2005 SZEWDIE1 00000021 500252 10880979

01 FC:1806 180.00 DA

This Information Disclosure Statement is being filed:

- within three months of the filing date of the application, or date of entry into the national stage of an international application, or before the mailing date of a first office action on the merits, whichever event last occurred;
- before the mailing of a first official action after filing of a request for continued examination (RCE) under 37 C.F.R. § 1.114;
- after three months of the filing date of this national application or the date of entry of the national stage in an international application, or after the mailing date of the first official action on the merits, whichever event last occurred, but before that mailing date of the first office action to occur of either: (1) a final action under 37 C.F.R. § 1.113; or (2) an action that otherwise closes prosecution in the application, and:
 - attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR
 - Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:
 - each item of the information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement;
- OR
 - no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement.
- on or before the payment of the issue fee but after the mailing date of the first to occur of either: (1) a final action under 37 C.F.R. § 1.113; (2) a notice of

allowance under 37 C.F.R. § 1.311; or (3) an action that otherwise closes prosecution in the application, and:

Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;

OR

no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement. AND

attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

after the payment of the issue fee. Applicant requests that the information contained in this Information Disclosure Statement be placed in the file according to 37 C.F.R. § 1.97(i), although the information may not be considered by the USPTO.

Enclosed is a copy of each listed reference that may be material to the examination of this application, and for which there may be a duty to disclose.

This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application No. , filed on , and the references cited therein are hereby referenced, but are not required to be provided in this application under 37 C.F.R. § 1.98(d).

This application was filed after June 30, 2003. Therefore, pursuant to the waiver of the requirements under 37 C.F.R. § 1.98(a)(2)(i), copies of each U.S. Patent and each

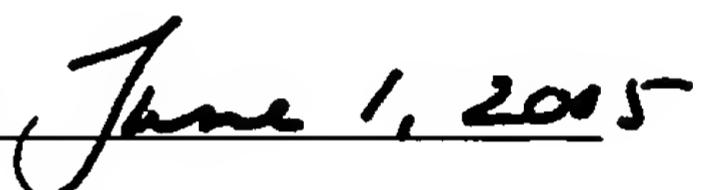
U.S. Patent Application Publication are not required to be submitted. Copies of any foreign patent documents and non-patent literature cited herein are enclosed.

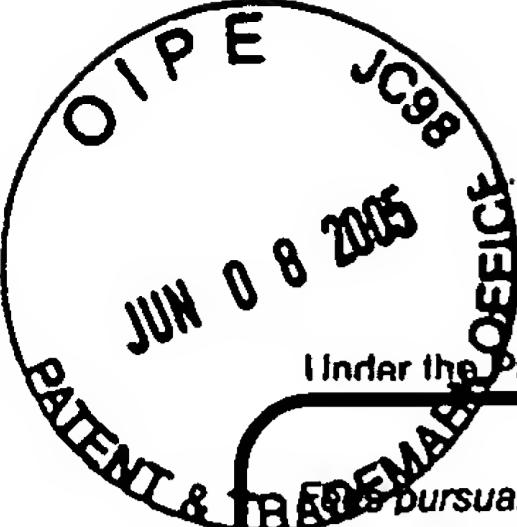
- Each item of information contained in this Information Disclosure Statement was cited in the communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this Information Disclosure Statement 37 C.F.R. § 1.704(d).
- Applicant submits that no fee is required for the consideration of this Information Disclosure Statement. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account No 500252 referencing case number . Consideration of the listed references and favorable action are solicited.

Respectively Submitted,


Colleen J. McKiernan
Registration No.: 48,570
Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008

Dated:





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Effective on 12/08/2004.

Pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2005

 Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$ 180.00)

Complete if Known

Application Number	10/080,979
Filing Date	February 22, 2002
First Named Inventor	Phillip Dan Cook
Examiner Name	Amy Hudson Bowman
Art Unit	1635
Attorney Docket No.	ISIS-5028

METHOD OF PAYMENT (check all that apply)

Check Credit Card Money Order None Other (please identify): _____

Deposit Account Deposit Account Number: 50-0252 Deposit Account Name: Isis Pharmaceuticals, Inc.

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

Charge fee(s) indicated below Charge fee(s) indicated below, except for the filing fee

Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 Credit any overpayments

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity	Fee (\$)	Small Entity	Fee (\$)	Small Entity	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description

Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent 50 25

Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent 200 100

Multiple dependent claims 360 180

Total Claims	Extra Claims	Fee (\$)	Fee Paid (\$)	Multiple Dependent Claims	Small Entity
- 20 or HP =	x	=		Fee (\$)	Fee (\$)
HP = highest number of total claims paid for, if greater than 20					

Indep. Claims	Extra Claims	Fee (\$)	Fee Paid (\$)
- 3 or HP =	x	=	

HP = highest number of independent claims paid for, if greater than 3

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
- 100 =	/ 50 =	(round up to a whole number) x	=	

4. OTHER FEE(S)

Non-English Specification, \$130 fee (no small entity discount)

Other: Supplemental IDS 180.00

SUBMITTED BY

Signature		Registration No. 48,570 (Attorney/Agent)	Telephone (760) 931-9200
Name (Print/Type)	Colleen J. McKiernan	Date	

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



PTO/SB/08a (08-03)

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Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
AA	US-3,687,808		08-29-1972	Merigan, Jr. et al.	
AB	US-4,605,735		08-12-1986	Miyoshi et al.	
AC	US-4,689,320		08-25-1987	Kaji	
AD	US-4,743,535		05-10-1988	Carrico	
AE	US-4,806,463		02-21-1989	Goodchild et al.	
AF	US-4,835,263		05-30-1989	Nguyen et al.	
AG	US-4,904,582		02-27-1990	Tullis	
AH	US-4,910,300		03-20-1990	Urdea et al.	
AI	US-4,958,013		09-18-1990	Letsinger	
AJ	US-5,015,733		05-14-1991	Smith et al.	
AK	US-5,034,506		07-23-1991	Summerton et al.	
AL	US-5,087,617		02-11-1992	Smith	
AM	US-5,098,890		03-24-1992	Gewirtz et al.	
AN	US-5,108,921		04-28-1992	Low et al.	
AO	US-5,135,917		08-04-1992	Burch	
AP	US-5,138,045		08-11-1992	Cook et al.	
AQ	US-5,166,195		11-24-1992	Ecker	
AR	US-5,194,428		03-16-1993	Agrawal et al.	
AS	US-5,212,295		05-18-1993	Cook	
AT	US-5,218,105		06-08-1993	Cook et al.	

FOREIGN PATENT DOCUMENTS

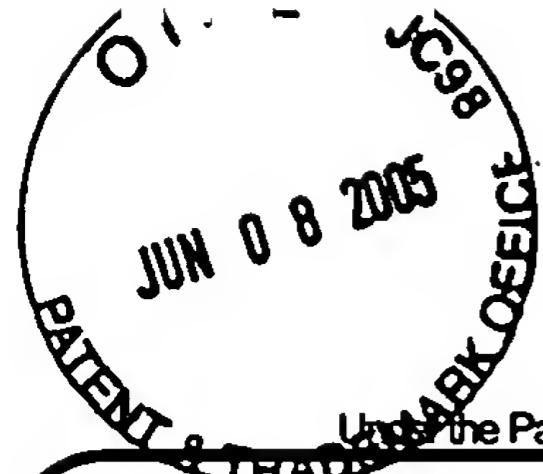
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ³
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
AU		EP 0 251 283 A2	01-07-1998	Wakunaga		
AV		WO 86/02929	05-22-1986	Life Technologies		
AW		WO 89/02931	04-06-1989	Cetus Corp.		
AX		WO 89/12060	12-14-1989	Benner		
AY		WO 90/10448	09-20-1990	Genentech Inc.		
AZ		WO 90/13300	11-15-1990	Biogen Inc.		
BA		WO 91/00243	01-10-1991	Union Oil Co.		
BB		WO 91/14696	10-03-1991	Gilead Sciences		
BC		WO 91/15500	10-17-1991	Du Pont		
BD		WO 92/05186	04-02-1992	Gilead Sciences		
BE		WO 95/06659	03-09-1995	Isis Pharm.		

Examiner Signature

Date Considered

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman
Attorney Docket Number	ISIS-5028

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Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
	BF	US-5,223,618	06-29-1993	Cook et al.	
	BG	US-5,242,906	09-07-1993	Pagano et al.	
	BH	US-5,264,423	11-23-1993	Cohen et al.	
	BI	US-5,272,263	12-21-1993	Hession et al.	
	BJ	US-5,276,019	01-04-1994	Cohen et al.	
	BK	US-5,284,931	02-08-1994	Springer et al.	
	BL	US-5,286,717	02-15-1994	Cohen et al.	
	BM	US-5,324,654	06-28-1994	Bredesen	
	BN	US-5,378,825	01-03-1995	Cook et al.	
	BO	US-5,386,023	01-31-1995	Sanghvi et al.	
	BP	US-5,457,191	10-10-1995	Cook et al.	
	BQ	US-5,459,255	10-17-1995	Cook et al.	
	BR	US-5,466,786	11-14-1995	Buhr et al.	
	BS	US-5,470,967	11-28-1995	Huie et al.	
	BT	US-5,506,351	04-09-1996	McGee	
	BU	US-5,510,239	04-23-1996	Baracchini et al.	
	BV	US-5,514,788	05-07-1996	Bennett et al.	
	BW	US-5,521,302	05-28-1996	Cook	
	BX	US-5,539,082	07-23-1996	Nielsen et al.	
	BY	US-5,541,307	07-30-1996	Cook et al.	
	BZ	US-5,554,746	09-10-1996	Ravikumar et al.	
	CA	US-5,571,902	11-05-1996	Ravikumar et al.	
	CB	US-5,578,718	11-26-1996	Cook et al.	
	CC	US-5,580,969	12-03-1996	Hoke et al.	
	CD	US-5,585,479	12-17-1996	Hoke et al.	
	CE	US-5,587,361	12-24-1996	Cook et al.	
	CF	US-5,587,469	12-24-1996	Cook et al.	
	CG	US-5,587,470	12-24-1996	Cook et al.	

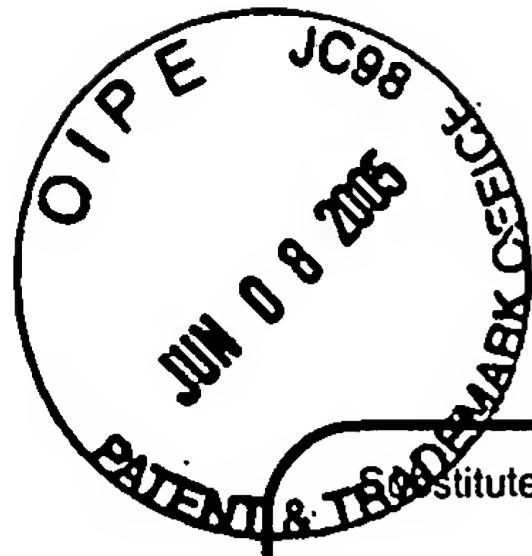
FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
	CH	WO 96/02556	02-01-1996	Hybridon Inc.		

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 27

U.S. PATENT DOCUMENTS

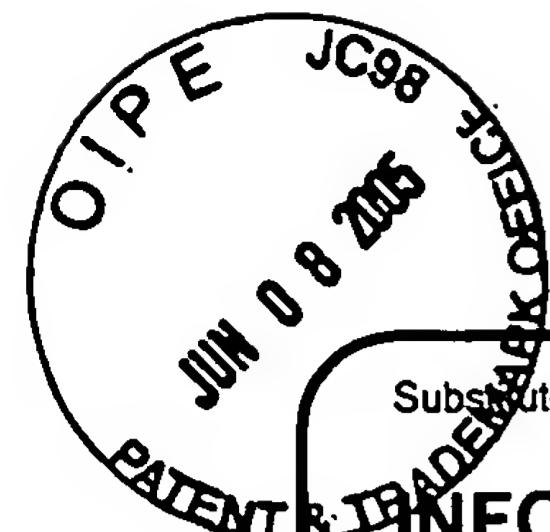
FOREIGN PATENT DOCUMENTS

Examiner Signature		Date Considered	
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WIPO Standard ST. 16 If possible. Applicant is to place a check mark here if English language Translation is attached.
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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

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of

27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number

ISIS-5028

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	CS	ADAMS, D. H. et al., "Intercellular Adhesion Molecule 1 on Liver Allografts During Rejection," <i>Lancet</i> (1989) 334(8672): 1122-1125.	
	CT	AGARWAL, K. L. et al., "Synthesis and enzymatic properties of deoxyribooligonucleotides containing methyl and phenylphosphonate linkages," <i>Nucleic Acids Research</i> (1979) 6(9):3009-3024.	
	CU	AGRAWAL, S. et al., "Oligodeoxynucleoside phosphoramidates and phosphorothioates as inhibitors of human immunodeficiency virus," <i>Proc. Natl. Acad. Sci. USA</i> (1988) 85:7079-7083.	
	CV	AGRAWAL, S., "Functionalization of Oligonucleotides with Amino Groups and Attachment of Amino Specific Reporter Groups," <i>Methods in Molecular Biology</i> (1994) vol. 26, Chapter 3, Human Press Inc., Totowa, NJ, pp. 93-120.	
	CW	AGRIS, C. H. et al., "Inhibition of Vesicular Stomatitis Virus Protein Synthesis and Infection by Sequence-Specific Oligodeoxyribonucleotide Methylphosphonates," <i>Biochemistry</i> (1986) 25(20):6268-6275.	
	CX	AKHTAR, S. et al., "Cellular uptake and intracellular fate of antisense oligonucleotides," <i>Trends in Cell Biol.</i> (1992) 2: 139-144.	
	CY	ALAHARI, S. K. et al., "The fission yeast <i>prp4</i> ⁺ gene involved in pre-mRNA splicing codes for a predicted serine/threonine kinase and is essential for growth," <i>Nucl. Acids Res.</i> (1993) 21(17):4079-4083.	
	CZ	ANDERSON, D. C. et al., "Leukocyte Adhesion Deficiency: An Inherited Defect in the Mac-1, LFA-1, and p150,95 Glycoproteins," <i>Ann. Rev. Med.</i> (1987) 38: 175-194.	
	DA	ARNOTT, S. et al., "Optimized Parameters for A-DNA and B-DNA," <i>Biochemical and Biophysical Research Communication</i> (1972) 47(6):1504-1510.	
	DB	ASSELINE, U. et al., "Nucleic acid-binding molecules with high affinity and base sequence specificity: Intercalating agents covalently linked to oligodeoxynucleotides," <i>Proc. Natl. Acad. Sci. USA</i> (1984) 81:3297-3301.	
	DC	ASSELINE, U. et al., "Solid-Phase Preparation of 5',3'-Heterobifunctional Oligodeoxyribonucleotides Using Modified Solid Supports," <i>Tetrahedron</i> (1992) 48: 1233-1254.	
	DD	ATHERTON, E. et al., "The Fluorenylmethoxycarbonyl Amino Protecting Group," <i>The Peptides</i> (1987) Gross and Meienhofer (eds.), Academic Press, New York, vol. 9:1-38.	

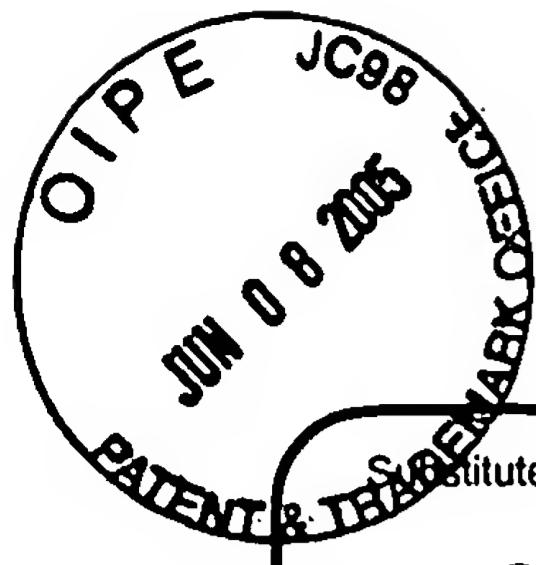
Examiner Signature

Date Considered

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¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

5 of 27

Complete if Known	
Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman
Attorney Docket Number	ISIS-5028

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	DE	BAKER, B.F., "Decapitation of a 5'-Capped Oligoribonucleotide by o-Phenanthroline: CU(II)," <i>J. Am. Chem. Soc.</i> (1993) 115(8):3378-3379.	
	DF	BALABAN, I. et al., "Bromo-derivatives of Glyoxaline," <i>Journal of Chemical Society</i> (1922) 121: 947-958.	
	DG	BEAUCAGE, S. L. et al., "Advances in the Synthesis of Oligonucleotides by the Phosphoramidite Approach," <i>Tetrahedron</i> (1992) 48(12):2223-2311.	
	DH	BEAUCAGE, S. et al., "Deoxynucleoside Phosphoramidites-A New Class of Key Intermediates for Deoxypolynucleotide Synthesis," <i>Tetrahedron Letters</i> (1981) 22(20): 1859-1862.	
	DI	BENNETT, C. F. et al., "Cationic Lipids Enhance Cellular Uptake and Activity of Phosphorothioate Antisense Oligonucleotides," <i>Mol. Pharm.</i> (1992) 41:1023-1033.	
	DJ	BERKOW, R. et al. (eds.), "Oncology," <i>The Merck Manual of Diagnosis and Therapy</i> (1987) 15th ed., Merck Sharp & Dohm Res. Lab., Rahway, NJ, pp. 1206-1228.	
	DK	BETEBENNER, D.A. et al., "Hepatobiliary Delivery of Polyaminopolycarboxylate Chelates: Synthesis and Characterization of a Cholic Acid Conjugate of EDTA and Biodistribution and Imaging Studies with Its Indium-111 Chelate," <i>Bioconjugate Chem.</i> (1991) 2(2):117-123.	
	DL	BEVILACQUA, M. P. et al., "Endothelial Leukocyte Adhesion Molecule 1: An Inducible Receptor for Neutrophils Related to Complement Regulatory Proteins and Lectins," <i>Science</i> (1989) 243: 1160-1165.	
	DM	BEVILACQUA, M. P. et al., "Identification of an inducible endothelial-leukocyte adhesion molecule," <i>Proc. Natl. Acad. Sci. USA</i> (1987) 84:9238-9242.	
	DN	BHAT, C., "2-Deoxy-3,5-di-O-p-toloyl-D-erythro-pentosyl Chloride," <i>Synthetic Procedures in Nucleic Acid Chemistry</i> (1968) Zorbach, W. W. and Tipson, R. S. (eds.), Interscience Publishers, New York, pp. 521-522.	
	DO	BHAT, V. et al., "A Simple and Convenient Method for the Selective N-Acylations of Cytosine Nucleosides," <i>Nucleosides & Nucleotides</i> (1989) 8(2): 179-183.	
	DP	BIGGADIKE, K. et al., "Short convergent route to homochiral carbocyclic 2'-deoxynucleosides and carbocyclic ribonucleosides," <i>J. Chem. Soc. Chem. Comm.</i> (1987):1083-1084.	
	DQ	BISCHOFF, R. et al., "Introduction of 5'-Terminal Functional Groups into Synthetic Oligonucleotides for Selective Immobilization," <i>Anal. Biochem.</i> (1987) 164: 336-344.	

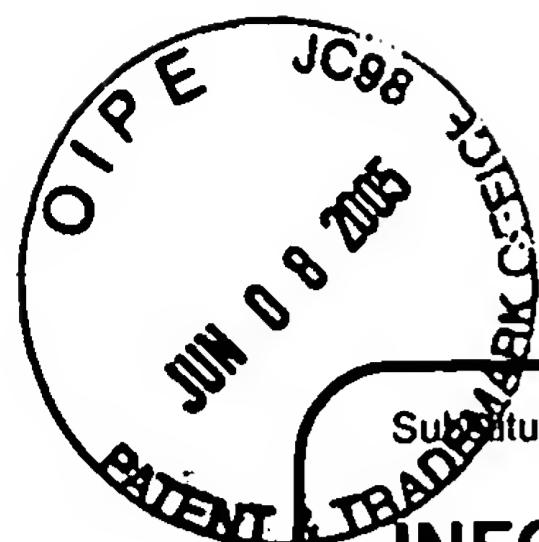
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Sheet 6 of 27

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	DR	BLACKBURN, G. et al., "Studies in Phosphorylation. Part XXIX. The Synthesis of Dialkyl Phosphates from Monoalkyl Phosphonates: Direct Oxidative Esterification," <i>J. Chem. Soc.</i> (1966): 239-245.	
	DS	BLUM, H. et al., "Inhibition of Hepatitis B Virus by Antisense Oligodeoxynucleotides," <i>Lancet</i> (1991) 337(8751): 1230.	
	DT	BOCHNER, B.S. et al., "Adhesion of Human Basophils, Eosinophils, and Neutrophils to Interleukin 1-activated Human Vascular Endothelial Cells: Contributions of Endothelial Cell Adhesion Molecules," <i>J. Exp. Med.</i> (1991) 173:1553-1556.	
	DU	BOUTORIN, A.S. et al., "Synthesis of alkylating oligonucleotide derivatives containing cholesterol or phenazinium residues at their 3'-terminus and their interaction with DNA within mammalian cells," <i>FEBS Letts.</i> (1989) 254(1,2):129-132.	
	DV	BRADLEY, G. et al., "P-glycoprotein, multidrug resistance and tumor progression," <i>Cancer Metastasis Rev.</i> (1994) 13: 223-233.	
	DW	BRANCH, A. D., "A Hitchhiker's Guide to Antisense and Nonantisense Biochemical Pathways," <i>Hepatology</i> (1996) 24(6): 1517-1529.	
	DZ	BRIGSTOCK, D. R. et al., "Species-Specific High Molecular Weight Forms of Basic Fibroblast Growth Factor," <i>Growth Factors</i> (1990) 4: 45-52.	
	EA	BRILL, W. K.-D. et al., "Synthesis of Oligodeoxynucleoside Phosphorodithioates via Thioamidites," <i>J. Am. Chem. Soc.</i> (1989) 111:2321-2322.	
	EB	BUTKE, G. et al., "Facile Synthesis of 2'-Amino-2'-Deoxyadenosine," <i>J. Carbohydrates Nucleosides & Nucleotides</i> (1980) 7(1): 63-75.	
	EC	BUTKE, G. et al., "Facile Synthesis of 2'-Amino-2'-deoxynucleoside from the Corresponding Arabino Derivative," <i>Nucleic Acid Chemistry</i> (1986) Part 3, Townsend, L.B. et al. (Eds.), John Wiley and Sons, New York, 149-152.	
	ED	CALVO-MATEO, A. et al., "3'-C-Cyano-3'-Deoxythymidine," <i>Tetrahedron Letters</i> (1988) 29(8): 941-944.	
	EE	CAMPBELL, I. L. et al., "Intercellular adhesion molecule 1 is induced on isolated endocrine islet cells by cytokines but not by reovirus infection," <i>Proc. Natl. Acad. Sci. USA</i> (1989) 86:4282-4256.	

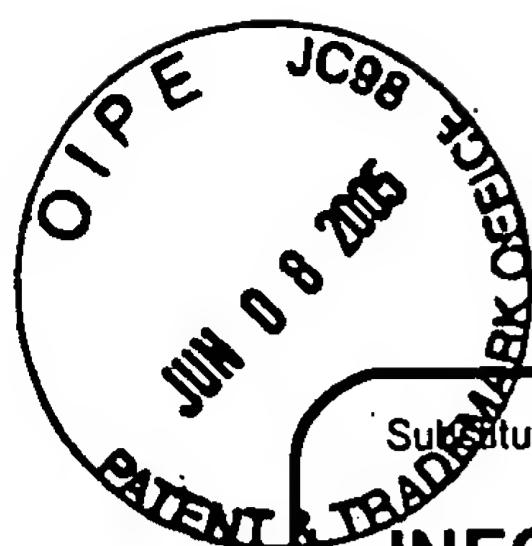
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 7 of 27

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<i>Application Number</i>	10/080,979
<i>Filing Date</i>	02/22/2002
<i>First Named Inventor</i>	Phillip Dan Cook
<i>Art Unit</i>	1635
<i>Examiner Name</i>	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

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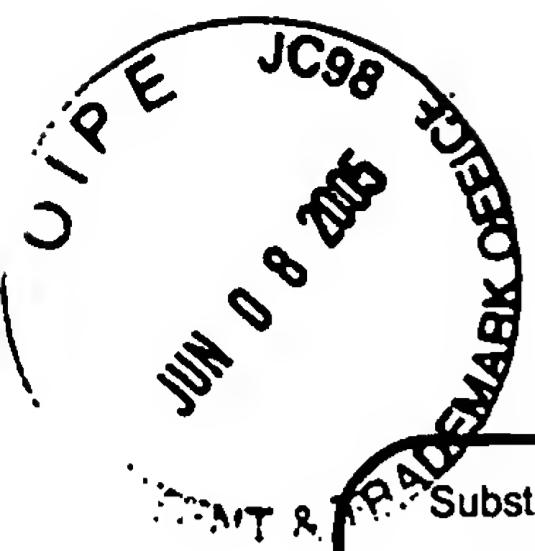
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	EF	CARLOS, T. et al., "Human Monocytes Bind to Two Cytokine-Induced Adhesive Ligands on Cultured Human Endothelial Cells: Endothelial-Leukocyte Adhesion Molecule-1 and Vascular Cell Adhesion Molecule-1," <i>Blood</i> (1991) 77(10):2266-2271.	
	EG	CARUTHERS, M. H., "Synthesis of Oligonucleotides and Oligonucleotide Analogues," <i>Oligonucleotides. Antisense Inhibitors of Gene Expression</i> , Cohen, J. S., ed., CRC Press, Inc., Boca Raton (1989) pp 7-24.	
	EH	CASTLE, R. N. et al., "Imidazo[4,5- <i>d</i>]pyridazines. I. Synthesis of 4,7-Disubstituted Derivatives," <i>J. Org. Chem.</i> (1958) 23:1534-1538.	
	EI	CAZENAVE, C. et al., "Enzymatic amplification of translation inhibition of rabbit β -globin mRNA mediated by anti-messenger oligodeoxynucleotides covalently linked to intercalating agents," <i>Nucl. Acids Res.</i> (1987) 15(12):4717-4736.	
	EJ	CHABNER, B. A. et al., "Reversal of Multidrug Resistance," <i>J. Clin. Oncol.</i> (1991) 9(1): 4-6.	
	EK	CHEN, C.-J. et al., "Genomic Organization of the Human Multidrug Resistance (MDR1) Gene and Origin of P-glycoproteins," <i>J. Biol. Chem.</i> (1990) 265(1):506-514.	
	EL	CHEN, S.-F. et al., "Mechanism of Action of the Novel Anticancer Agent 6-Fluoro-2-(2'-fluoro-1,1'-biphenyl-4-yl)-3-methyl-4-quinolinecarboxylic Acid Sodium Salt (NSC 368390): Inhibition of <i>de Novo</i> Pyrimidine Nucleotide Biosynthesis," <i>Cancer Res.</i> (1986) 46: 5014-5019.	
	EM	CHEN, C. et al., "Internal Duplication and Homology with Bacterial Transport Proteins in the <i>mdr1</i> (P-Glycoprotein) Gene from Multidrug-Resistant Human Cells," <i>Cell</i> (1986) 47: 381-389.	
	EN	CHEN, Y et al., "Studies on Fluoroalkylation and Fluoroalkoxylation. Part 33. Direct Trifluoromethylation of Aryl Halides with Fluorosulphonyldifluoromethyl Iodide in the Presence of Copper: an Electron Transfer Induced Process," <i>J. Chem. Soc. Perkin Transactions I</i> (1989) 2385-2387.	
	EO	CHIANG, M.-Y. et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," <i>J. Biol. Chem.</i> (1991) 266(27): 18162-18171.	
	EP	CHIRGIN, J. M. et al., "Isolation of Biologically Active Ribonucleic Acid from Sources Enriched in Ribonuclease," <i>Biochemistry</i> (1979) 18(24):5294-5299.	
	EQ	CHOLLET, A., "Selective Attachment of Oligonucleotides to Interleukin-1 β and Targeted Delivery to Cells," <i>Nucleosides & Nucleotides</i> (1990) 9(7): 957-966.	

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Sheet 8 of 27

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<i>Application Number</i>	10/080,979
<i>Filing Date</i>	02/22/2002
<i>First Named Inventor</i>	Phillip Dan Cook
<i>Art Unit</i>	1635
<i>Examiner Name</i>	Amy Hudson Bowman
<i>Attorney Docket Number</i>	ISIS-5028

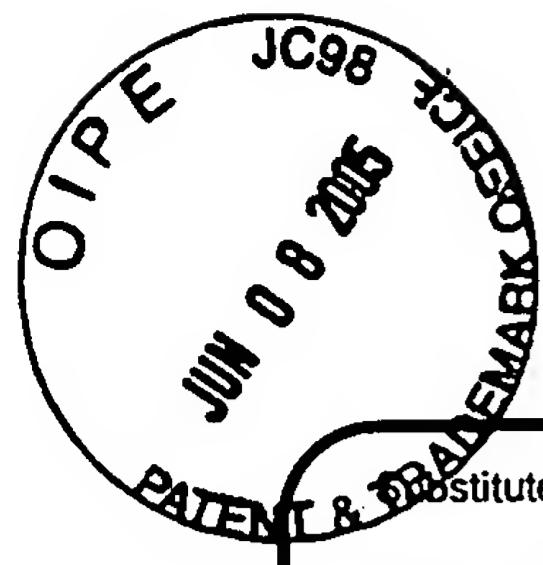
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	ER	CHOU, T.-C. et. al., "Quantitative Analysis of Dose-Effect Relationships: The Combined Effects of Multiple Drugs or Enzyme Inhibitors," <i>Adv. Enz. Regul.</i> (1984) 22: 27-55.		
	ES	CODINGTON, J. F. et al., "Nucleosides. XVIII. Synthesis of 2'-Fluorothymidine, 2'-Fluorodeoxyuridine, and Other 2'-Halogeno-2'-Deoxy Nucleosides," <i>J. Org. Chem.</i> (1964) 29: 558-564.		
*	ET	COHEN, J., in <i>Oligonucleotides: Antisense Inhibitors of Gene Expression</i> , CRC Press, Inc., Boca Raton, FL, 1989.		
	EU	CONSTANT, J. F. et al., "Heterodimeric Molecules Including Nucleic Acid Bases and 9-Aminoacridine. Spectroscopic Studies, Conformations and Interactions with DNA", <i>Biochemistry</i> (1988) 27(11):3997-4003.		
	EV	COOK, P. D. et al., "Synthesis and Antiviral and Enzymatic Studies of Certain 3-Deazaguanines and Their Imidazolecarboxamide Precursors," <i>J. Med. Chem.</i> (1978) 21(12):1212-1218.		
	EW	COONEY, M. et al., "Site-Specific Oligonucleotide Binding Represses Transcription of the Human c-myc Gene in Vitro," <i>Science</i> (1988) 241: 456-459.		
	EX	COREY, D. et al., "Generation of a Hybrid Sequence-Specific Single-Stranded Deoxyribonuclease," <i>Science</i> (1987) 238:1401-1403.		
	EY	COREY, D. et al., "Sequence-Selective Hydrolysis of Duplex DNA by an Oligonucleotide-Directed Nuclease," <i>J. Am. Chem. Soc.</i> (1989) 111(22):8523-8525.		
	EZ	CORRIAS, M. V. et al., "An Oligomer Complementary to the 5' End Region of MDR1 Gene Decreases Resistance to Doxorubicin of Human Adenocarcinoma-Resistant Cells," <i>Anticancer Res.</i> (1992) 12: 1431-1438.		
	FA	COSIMI, A. B. et al., "In Vivo Effects of Monoclonal Antibody to ICAM-1 (CD54) in Nonhuman Primates with Renal Allografts," <i>J. Immunol.</i> (1990) 144(12): 4604-4612.		
	FB	CROOKE, S. T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice," <i>J. Pharmacol Exp. Ther.</i> (1996) 277(2):923-937.		
	FC	CROOKE, S. T. et al., "Progress in the development and patenting of antisense drug discovery technology," <i>Exp. Opin. Ther. Patents</i> (1996) 6(9): 855-870.		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				<i>Application Number</i>	10/080,979
				<i>Filing Date</i>	02/22/2002
				<i>First Named Inventor</i>	Phillip Dan Cook
				<i>Art Unit</i>	1635
				<i>Examiner Name</i>	Amy Hudson Bowman
Sheet	9	of	27	<i>Attorney Docket Number</i>	ISIS-5028

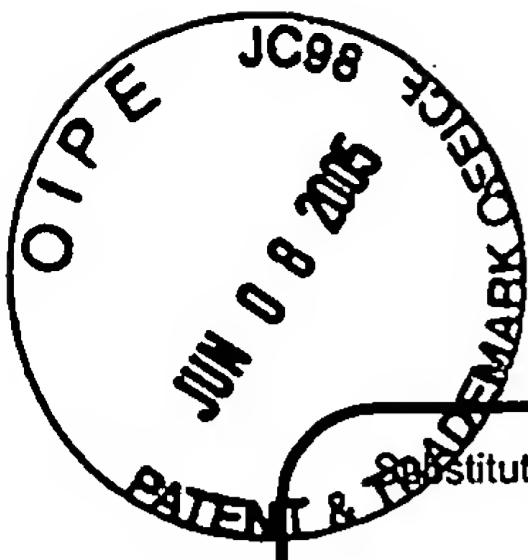
NON PATENT LITERATURE DOCUMENTS				
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	FD	DAMHA, M. J. et al., "Solution and solid phase chemical synthesis of arabinonucleotides," <i>Can. J. Chem.</i> (1989) 67: 831-839.		T ²
	FE	DAMHA, M. J. et al., "An improved procedure for derivatization of controlled-pore glass beads for solid-phase oligonucleotide synthesis," <i>Nucleic Acids Res.</i> (1990) 18(13): 3813-3821.		
	FG	DAVES, G. et al., "The Chemistry and Biochemistry of C-Nucleosides," <i>Progress in Medicinal Chemistry</i> (1976) 13: 304-349.		
	FH	DE SMIDT, P.C. et al., "Association of antisense oligonucleotides with lipoproteins prolongs the plasma half-life and modifies the tissue distribution", <i>Nucl. Acids Res.</i> (1991) 19(17):4695-4700.		
	FI	DE VIRGILIO, C. et al., "Cloning and Disruption of a Gene Required for Growth on Acetate but not on Ethanol: the Acetyl-Coenzyme A Synthetase Gene of <i>Saccharomyces cerevisiae</i> ," <i>Yeast</i> (1992) 8: 1043-1051.		
	FJ	DEAN, N. M. et al., "Inhibition of Protein Kinase C- α Expression in Human A549 Cells by Antisense Oligonucleotides Inhibits Induction of Intercellular Adhesion Molecule 1 (ICAM-1) mRNA by Phorbol Esters," <i>J. Biol. Chem.</i> (1994) 269(23): 16416-16424.		
	FK	DELGADO, C. et al, "The Uses and Properties of PEG-Linked Proteins," <i>Critical Reviews in Therapeutic Drug Carrier Systems</i> (1992) 9(3,4):249-304.		
	FL	DINGWALL, C. et al., "Protein Import Into the Cell Nucleus," <i>Ann. Rev. Cell Biol.</i> (1986) 2: 367-390.		
	FM	DIVAKAR, K. J. et al., "4-(1,2,4-Triazol-1-yl)-and 4-(3-Nitro-1,2,4-triazol-1-yl)-1-(β -D-2,3,5-tri-O-acetylarabinofuranosyl)pyrimidin-2(1 <i>H</i>)-ones. Valuable Intermediates in the Synthesis of Derivatives of 1-(β -D-Arabinofuranosyl)cytosine (Ara-C)," <i>J. Chem. Soc. Perkin Trans I</i> (1982) 1171-1176.		
	FN	DIZIO, J. et al., "Progesterin-Rhenium Complexes: Metal-Labeled Steroids with High Receptor Binding Affinity, Potential Receptor-Directed Agents for Diagnostic of Imaging or Therapy," <i>Bioconjugate Chem.</i> (1991) 2(5):353-366.		
	FO	DOAN, P. L. et al., "Sequence-targeted chemical modifications of nucleic acids by complementary oligonucleotides covalently linked to porphyrins," <i>Nucl. Acids Res.</i> (1987) 15(21):8643-8659.		
	FP	DREYER, G. et al., "Sequence-specific cleavage of single-stranded DNA: Oligodeoxynucleotide-EDTA·Fe(II)," <i>Proc. Natl. Acad. Sci. USA</i> (1985) 82:968-972. Correction (1985) 82: 3532.		

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Sheet

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	FQ	DUSTIN, M. L. et al., "Lymphocyte Function-associated Antigen-1 (LFA-1) Interaction with Intercellular Adhesion Molecule-1 (ICAM-1) is One of At Least Three Mechanisms for Lymphocyte Adhesion to Cultured Endothelial Cells", <i>J. Cell Biol.</i> (1987) 107:321-331.	
	FR	ECKSTEIN, F. et al., "Polynucleotides Containing 2'-Chloro-2'-Deoxyribose," <i>Biochemistry</i> (1972) 11(23):4336-4344.	
	FS	EDER, P. S. et al., "Substrate Specificity and Kinetics of Degradation of Antisense Oligonucleotides by a 3' Exonuclease in Plasma," <i>Antisense Res. Dev.</i> (1991) 1: 141-151.	
	FT	EFFERTH, T. et al., "Modulation of P-Glycoprotein-Mediated Multidrug Resistance by Monoclonal Antibodies, Immunotoxins or Antisense Oligodeoxynucleotides in Kidney Carcinoma and Normal Kidney Cells," <i>Oncology</i> (1993) 50: 303-308.	
	FU	EGHOLM, M. et al., "Peptide Nucleic Acids (PNA). Oligonucleotide Analogues with an Achiral Peptide Backbone," <i>J. Am. Chem. Soc.</i> (1992) 114(5):1895-1897.	
	FV	ENGLISCH, U. et al., "Chemically Modified Oligonucleotides as Probes and Inhibitors," <i>Angew. Chem. Int. Ed. Eng.</i> (1991) 30(6):613-722.	
	FW	FAULL, R. J. et al., "Tubular Expression of Intercellular Adhesion Molecule-1 During Renal Allograft Rejection," <i>Transplantation</i> (1989) 48(2): 226-230.	
	FX	FERENTZ, A. E. et al., "Disulfide Cross-Linked Oligonucleotides," <i>J. Am. Chem. Soc.</i> (1991) 113(10): 4000-4002.	
	FY	FIDANZA, J. A. et al., "Site-Specific Labeling of DNA Sequences Containing Phosphorothioate Diesters," <i>J. Am. Chem. Soc.</i> (1992) 114(14):5509-5517.	
	FZ	FIDANZA, J. A. et al., "Use of a Thiol Tether for the Site-Specific Attachment of Reporter Groups to DNA," <i>J. Org. Chem.</i> (1992) 57(8): 2340-2346.	
	GA	FRENCH, T. J. et al., "Expression of Two Related Nonstructural Proteins of Bluetongue Virus (BTV) Type 10 in Insect Cells by a Recombinant Baculovirus: Production of Polyclonal Ascitic Fluid and Characterization of the Gene Product in BTV-Infected BHK Cells," <i>J. Virology</i> (1989) 63(8): 3270-3278.	
	GB	FRESKOS, J., "Synthesis of 2'-Deoxypyrimidine Nucleosides Via Copper (I) Iodide Catalysis," <i>Nucleosides & Nucleotides</i> (1989) 8(5&6): 1075-1076.	
	GC	FROEHLER, B. et al., "Synthesis of DNA via deoxynucleoside H-phosphonate intermediates", <i>Nucleic Acids Research</i> (1986) 14(13): 5399-5407.	

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number

ISIS-5028

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	GD	FROHMAN, E. M. et al., "The induction of intercellular adhesion molecule 1 (ICAM-1) expression on human fetal astrocytes by interferon-γ, tumor necrosis factor α, lymphotoxin, and interleukin-1: relevance to intracerebral antigen presentation," <i>J. Neuroimmunol</i> (1989) 23: 117-124.	
	GE	GAFFNEY, B. et al., "A New Strategy for the Protection of Deoxyguanosine During Oligonucleotide Synthesis," <i>Tetrahedron Letters</i> (1982) 23(22): 2257-2260.	
*	GF	GAIT, M. J., "Oligonucleotide Synthesis", IRL Press, 1985	
	GG	GAO, J. et al., "Cloning and Characterization of a Mouse Gene with Homology to the Human von Hippel-Lindau Disease Tumor Suppressor Gene: Implications for the Potential Organization of the Human von Hippel-Lindau Disease Gene," <i>Cancer Res.</i> (1995) 55: 743-747.	
	GH	GAUR, R. et al., "A simple method for the introduction of thiol group at 5'-termini of oligodeoxynucleotides," <i>Nucleic Acids Res.</i> (1989) 17(11): 4404.	
	GI	GELBERT, L. M. et al., "Analysis of GPT Activity in Mammalian Cells with a Chromosomally Integrated Shuttle Vector Containing Altered <i>gpt</i> Genes," <i>Som. Cell. Mol. Genet.</i> (1990) 16(2): 173-184.	
	GJ	GIBBS, W. W., "State of Shock: Sepsis can be fatal to firms as well as to patients," <i>Scientific American</i> (1994) Oct:133-134.	
	GK	GMEINER, W. H. et al., "Development of an Efficient Oligonucleotide Derivation Protocol," <i>Bioorg. Med. Chem. Letts.</i> (1991) 1(9): 487-490.	
	GL	GOLD, L. et al., "Translational Initiation," <i>Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology</i> (1987) American Society for Microbiology, Washington, D.C., 2: 1302-1307.	
	GM	GOODCHILD, J. et al., "Inhibition of human immunodeficiency virus replication by antisense oligodeoxynucleotides," <i>Proc. Natl. Acad. Sci. USA</i> (1988) 85: 5507-5511.	
	GN	GOODCHILD, J., "Conjugates of Oligonucleotides and Modified Oligonucleotides: A Review of Their Synthesis and Properties," <i>Bioconjugate Chemistry</i> (1990) 1(3):165-187.	
	GO	GOTTESMAN, M. M. et al., "The Multidrug Transporter, a Double-edged Sword," <i>J. Biol. Chem.</i> (1988) 263(25): 12163-12166.	

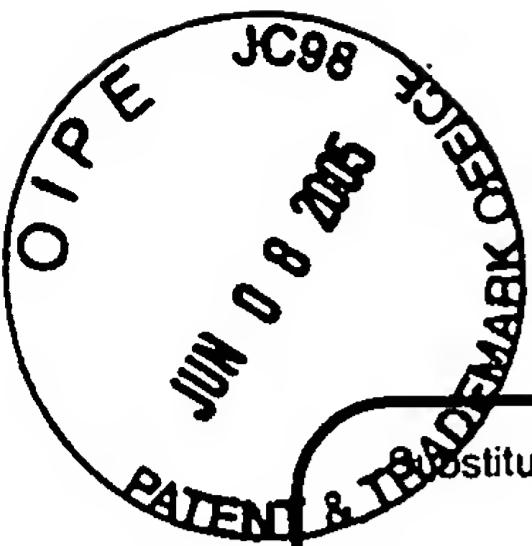
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Art Unit	1635
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Attorney Docket Number	ISIS-5028

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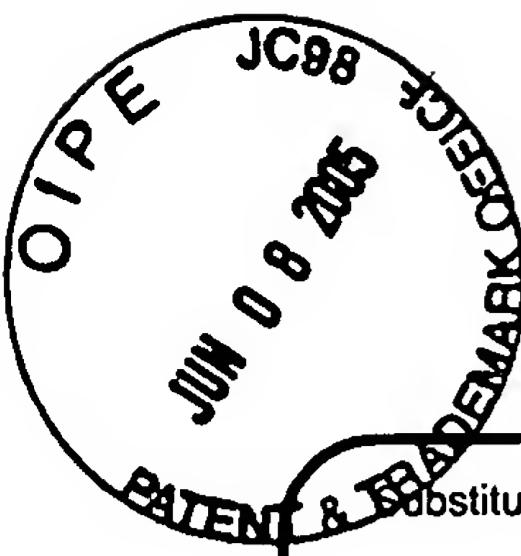
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	GP	GRAHAM, M. J. et al., "Tritium labeling of antisense oligonucleotides by exchange with tritiated water," <i>Nucleic Acids Res.</i> (1993) 21(16): 3737-3743.	
	GQ	GREENE, T. W. et al., "Protection for the Carbonyl Group," <i>Protective Groups in Organic Synthesis</i> , 2nd ed., (1991) John Wiley & Sons, New York, pp. 178-223.	
	GR	GREENFIELD, L. et al., "Thiol-Containing Cross-Linking Agent with Enhanced Steric Hindrance," <i>Bioconjugate Chem.</i> (1990) 1(6): 400-410.	
	GS	GREVE, J. M. et al., "The Major Human Rhinovirus Receptor is ICAM-1," <i>Cell</i> (1989) 56: 839-847.	
	GT	GRIFFITHS, C. E. M. et al., "Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1) Expression Precedes Dermal T Lymphocytic Infiltration in Allergic Contact Dermatitis (<i>Rhus dermatitis</i>)," <i>Am. J. Pathology</i> . (1989) 135(6): 1045-1053.	
	GU	GUERRA, F. I. et al., "Synthetic 6-Glucosyl Phospholipid as a Drug Transport System," <i>Tetrahedron Letters</i> (1987) 28(31): 3581-3584.	
	GV	GUSCHLBAUER, W. et al, "Nucleoside conformation is determined by the electronegativity of the sugar substituent," <i>Nucleic Acids Research</i> (1980) 8(6):1421-1433.	
	GW	HALE, L. P. et al., "Immunohistologic Analysis of the Distribution of Cell Adhesion Molecules within the Inflammatory Synovial Microenvironment," <i>Arth. Rheum.</i> (1989) 32(1): 22-30.	
	GX	HANSSKE, F., "2'- and 3'-Ketonucleosides and their <i>Arabino</i> and <i>Xylo</i> Reduction Products," <i>Tetrahedron</i> (1984) 40: 125-135.	
	GY	HARALAMBIDIS, J. et al., "The Solid Phase Synthesis of Oligonucleotides Containing a 3'-Peptide Moiety," <i>Tetrahedron Letters</i> (1987) 28(43): 5199-5202.	
	GZ	HARALAMBIDIS, J. et al., "Preparation of base-modified nucleosides suitable for non-radioactive label attachment and their incorporation into synthetic oligodeoxyribonucleotides," <i>Nucleic Acids Research</i> (1987) 15(12):4857-4876.	
	HA	HARLAN, J. M., "Leukocyte-Endothelial Interactions," <i>Blood</i> (1985) 65(3): 513-525.	
	HB	HARRIS, C. et al., "New Strategy for the Synthesis of Oligodeoxynucleotides Bearing Adducts at Exocyclic Amino Sites of Purine Nucleosides," <i>J. Am. Chem. Soc.</i> (1991) 113: 4328-4329.	

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Attorney Docket Number	ISIS-5028

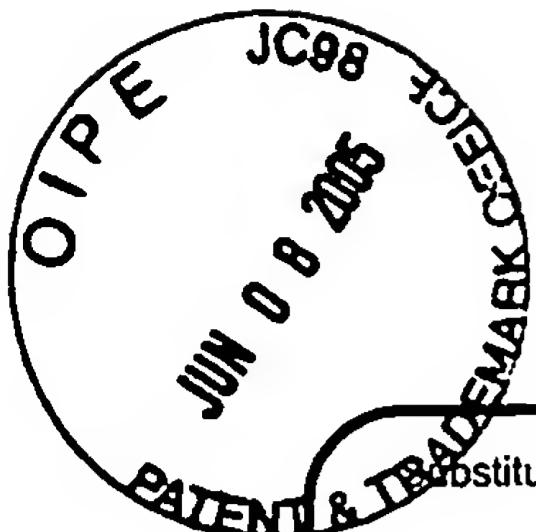
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	HC	HAUG, C. E. et al., "A Phase I Trial of Immunosuppression with Anti-ICAM-1 (CD54) mAb in Renal Allograft Recipients," <i>Transplantation</i> (1993) 55(4): 766-773.
	HD	HERTEL, L. W. et al., "Synthesis of 2-Deoxy-2,2-difluoro-D-ribose and 2-Deoxy-2,2-difluoro-D-ribofuranosyl Nucleosides," <i>J. Org. Chem.</i> (1988) 53(11): 2406-2409.
	HE	HO, S. P. et al., "Potent antisense oligonucleotides to the human multidrug resistance-1 mRNA are rationally selected by mapping RNA-accessible sites with oligonucleotide libraries," <i>Nucl. Acids Res.</i> (1996) 24(10): 1901-1907.
	HF	HO, V. C. et al., "Treatment of severe lichen planus with cyclosporine," <i>J. Am. Acad. Dermatol.</i> (1990) 22: 64-68.
	HG	HOTODA, H. et al., "Biologically Active Oligodeoxyribonucleotides - II: Structure Activity Relationships of Anti-HIV-1 Pentadecadeoxyribonucleotides Bearing 5'-End-Modifications," <i>Nucleosides & Nucleotides</i> (1994) 13(6&7): 1375-1395.
	HI	IKEHARA, M. et al., "Polynucleotides. LII. Synthesis and properties of poly (2'-deoxy-2'-fluoroadenyllic acid)," <i>Nucleic Acids Research</i> (1978) 5(6): 1877-1887.
	HJ	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides-LXXXIX., Purine Cyclonucleosides. (43). Synthesis and Properties of 2'-Halogen-2'-deoxyguanosines," <i>Chem. Pharm. Bull.</i> (1981) 29(11): 3281-3285.
	HK	IKEHARA, M. et al., "Polynucleotides. L. Synthesis and properties of poly (2'-chloro-2'-deoxyadenyllic acid) and poly (2'-bromo-2'-deoxyadenyllic acid)," <i>Nucleic Acids Research</i> (1977) 4(12): 4249-4260.
	HL	IKEHARA, M. et al., "Polynucleotides. LVI. Synthesis and properties of poly(2'-deoxy-2'-fluoroinosinic acid)," <i>Nucleic Acids Research</i> (1978) 5(9): 3315-3324.
	HM	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides-LXV," <i>Tetrahedron</i> (1975) 31: 1369-1372.
	HN	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides. LXXXVII. Purine Cyclonucleosides. XLII. Synthesis of 2'-Deoxy-2'-fluoroguanosine," <i>Chem. Pharm. Bull.</i> (1981) 29(4): 1034-1038.
	HO	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides-LXXIVI," <i>Tetrahedron</i> (1978) 34: 1133-1138.

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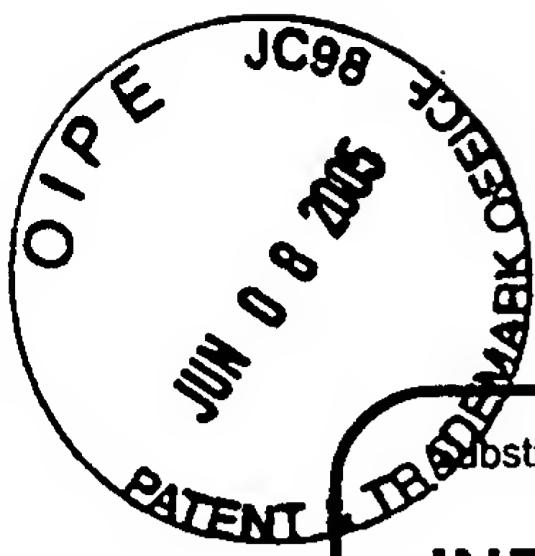
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	HP	IKEHARA, M., "Purine 8-Cyclonucleosides," <i>Accounts of Chemical Research</i> (1969) 2: 47-53.
	HQ	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides. LXXIX. Purine Cyclonucleosides. (37). The Total Synthesis of an Antibiotic 2'-Amino-2'-deoxyguanosine," <i>Chem. Pharm. Bull.</i> (1978) 26: 240-244.
	HR	IKEHARA, M. et al., "Studies of Nucleosides and Nucleotides. LXXXII. Cyclonucleosides. (39) Synthesis and Properties of 2'-Halogen-2'-deoxyadenosines," <i>Chem. Pharm. Bull.</i> (1978) 26: 2449-2453.
	HS	ING, N. H. et al., "In vivo transcription of a progesterone-responsive gene is specifically inhibited by a triplex-forming oligonucleotide," <i>Nucleic Acids Res.</i> (1993) 21(12): 2789-2796.
	HT	INOUE, H. et al., "Synthesis and hybridization studies on two complementary nona(2'-O-methyl)ribonucleotides," <i>Nucleic Acids Research</i> (1987) 15(15): 6131-6148.
	HU	ISHIDA, Y. et al., "Multidrug Resistance in Cultured Human Leukemia and Lymphoma Cell Lines Detected by a Monoclonal Antibody, MRK16," <i>Jpn. J. Cancer Res.</i> (1989) 80: 1006-1013.
	HV	ISOBE, M. et al., "Early Detection of Rejection and Assessment of Cyclosporine Therapy by ¹¹¹ In Antimyosin Imaging in Mouse Heart Allografts," <i>Circulation</i> (1991) 84: 1246-1255.
	HW	ISOBE, M. et al., "Specific Acceptance of Cardiac Allograft After Treatment with Antibodies to ICAM-1 and LFA-1," <i>Science</i> (1992) 255: 1125-1127.
	HX	IYER, R. et al., "3H-1,2-Benzodithiole-3-one, 1,1-Dioxide as an Improved Sulfurizing Reagent in the Solid-Phase Synthesis of Oligodeoxyribonucleoside Phosphorothioates," <i>J. Am. Chem. Soc.</i> (1990) 112: 1253-1254.
	HY	JABLONSKI, E. et al., "Preparation of oligodeoxynucleotide-alkaline phosphatase conjugates and their use as hybridization probes," <i>Nucleic Acid Research</i> (1986) 14(15): 6115-6128.
	HZ	JÄGER, A. et al., "Oligonucleotide N-Alkylphosphoramidates: Synthesis and Binding to Polynucleotides," <i>Biochemistry</i> (1988) 27(19): 7237-7246.
	JA	JAMES, W., "Towards gene-inhibition therapy: a review of progress and prospects in the field of antiviral antisense nucleic acids and ribozymes," <i>Antiviral Chem. Chemo.</i> (1991) 2(4): 191-214.
	JB	JARVI, E. T. et al., "Synthesis and Biological Evaluation of Dideoxynucleosides Containing a Difluoromethylene unit," <i>Nucleosides & Nucleotides</i> (1989) 8(5&6): 1111-1114.

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	JC	JAYARAMAN, K. et al., "Selective inhibition of <i>Escherichia coli</i> protein synthesis and growth by nonionic oligonucleotides complementary to the 3' end of 16S rRNA," <i>Proc. Natl. Acad. Sci. USA</i> (1981) 78(3): 1537-1541.		T ²
	JD	JONES, G. et al., "4'-Substituted Nucleosides. 5. Hydroxymethylation of Nucleoside 5'-Aldehydes," <i>J. Org. Chem.</i> (1979) 44(8): 1309-1317.		
	JE	JUBY, C. D. et al., "Facile Preparation of 3'Oligonucleotide-Peptide Conjugates," <i>Tetrahedron Letters</i> (1991) 32(7): 879-882.		
	JF	KABANOV, A. V. et al. "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells," <i>FEBS Letts.</i> (1990) 259(2): 327-330.		
	JG	KAHAN, B. D. et al., "The Synergistic Interactions in vitro and in vivo of Brequinar Sodium with Cyclosporine or Rapamycin Alone and in Triple Combination," <i>Transplantation</i> (1993) 55(4): 894-900.		
	JH	KAJIIJI, S. et al., "Structurally Distinct MDR Modulators Show Specific Patterns of Reversal against P-Glycoproteins Bearing Unique Mutations at Serine ^{939/941} ," <i>Biochemistry</i> (1994) 33(17): 5041-5048.		
	JI	KANAGASUNDARAM, V. et al., "Isolation and characterization of the gene encoding gluconolactonase from <i>Zymomonas mobilis</i> ," <i>Biochim. Biophys. Acta</i> (1992) 1171: 198-200.		
	JJ	KANE, S. E. et al., "A new vector using the human multidrug resistance gene as a selectable marker enables overexpression of foreign genes in eukaryotic cells," <i>Gene</i> (1989) 84: 439-446.		
	JK	KAZIMIERCZUK, Z. et al., "Synthesis of 2'-Deoxytubercidin, 2'-Deoxyadenosine, and Related 2'-Deoxynucleosides via a Novel Direct Stereospecific Sodium Salt Glycosylation Procedure," <i>J. Am. Chem. Soc.</i> (1984) 106(21): 6379-6382.		
	JL	KIBLER-HERZOG, L. et al., "Duplex stabilities of phosphorothioate, methylphosphonate, and RNA analogs of two DNA 14-mers," <i>Nucleic Acids Res.</i> (1991) 19(11): 2979-2986.		
	JM	KIEHNTOPF, M. et al., "Ribozyme-mediated cleavage of the MDR-1 transcript restores chemosensitivity in previously resistant cancer cells," <i>EMBO J.</i> (1994) 13(19): 4645-4652.		
	JN	KISHIMOTO, T. K. et al., "The Leukocyte Integrins," <i>Adv. Immunol.</i> (1989) 46: 149-182.		

Examiner Signature	Date Considered
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**INFORMATION DISCLOSURE
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Sheet

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Complete if Known

<i>Application Number</i>	10/080,979
<i>Filing Date</i>	02/22/2002
<i>First Named Inventor</i>	Phillip Dan Cook
<i>Art Unit</i>	1635
<i>Examiner Name</i>	Amy Hudson Bowman

Attorney Docket Number

ISIS-5028

NON PATENT LITERATURE DOCUMENTS

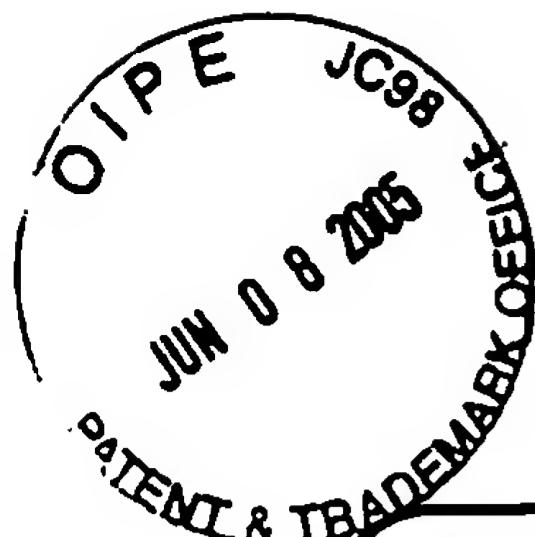
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	JO	KITAJIMA, I. et al., "Ablation of Transplanted HTLV-I Tax-Transformed Tumors in Mice by Antisense Inhibition of NF -κB," <i>Science</i> (1992) 258: 1792-1795.	
	JP	KNORRE, D. et al., "Complementary-Addressed (Sequence-Specific) Modification of Nucleic Acids," <i>Prog. Nucl. Acid Res. Mol. Biol.</i> (1985) 32: 291-321.	
	JQ	KOBAYASHI, H. et al., "Reversal of Drug Sensitivity in Multidrug-Resistant Tumor Cells by an MDR1 (PGY1) Ribozyme," <i>Cancer Res.</i> (1994) 54: 1271-1275.	
	JR	KOOLE, L. et al., "Synthesis of Phosphate-Methylated DNA Fragments Using 9-Fluorenylmethoxycarbonyl as Transient Base Protecting Group," <i>J. Org. Chem.</i> (1989) 54(7): 1657-1664.	
	JS	KRIEG, A. M. et al., "Modification of antisense phosphodiester oligonucleotides by a 5' cholestrylo moiety increases cellular association and improves efficacy," <i>Proc. Natl. Acad. Sci. USA</i> (1993) 90: 1048-1052.	
	JT	KRIEG, A. M. et al., "Uptake of Oligodeoxyribonucleotides by Lymphoid Cells Is Heterogeneous and Inducible," <i>Antisense Research and Development</i> (1991) 1: 161-171.	
	JU	LEMAITRE, M. et al., "Specific antiviral activity of a poly(L-lysine)-conjugated oligodeoxyribonucleotide sequence complementary to vesicular stomatitis virus N protein mRNA initiation site," <i>Proc. Natl. Acad. Sci. USA</i> (1987) 84: 648-652.	
	JV	LEONETTI, J. P. et al., "Biological Activity of OligonucleotidePoly(L-lysine) Conjugates: Mechanism of Cell Uptake," <i>Bioconjugate Chem.</i> (1990) 1(2): 149-153.	
	JW	LETSINGER, R. L. et al., "Effects of pendant groups at phosphorus on binding properties of d-ApA analogues," <i>Nucleic Acids Research</i> (1986) 14(8): 3487-3499.	
	JX	LETSINGER, R. L. et al., "Cholestrylo-conjugated oligonucleotides: synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," <i>Proc. Natl. Acad. Sci. USA</i> (1989) 86: 6553-6556.	
	JY	LISBY, S. et al., "Intercellular adhesion molecule-1 (ICAM-1) expression correlated to inflammation," <i>Br. J. Dermatol.</i> (1989) 120: 479-484.	
	JZ	LIU, J. et al., "Calcineurin Is a Common Target of Cyclophilin-Cyclosporin A and FKBP-FK506 Complexes," <i>Cell</i> (1991) 66: 807-815.	
	KA	LOOSE-MITCHELL, D., "Antisense nucleic acids as a potential class of pharmaceutical agents", <i>TIPS</i> (1988) 9: 45-47.	

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<i>Art Unit</i>	1635
<i>Examiner Name</i>	Amy Hudson Bowman

Attorney Docket Number

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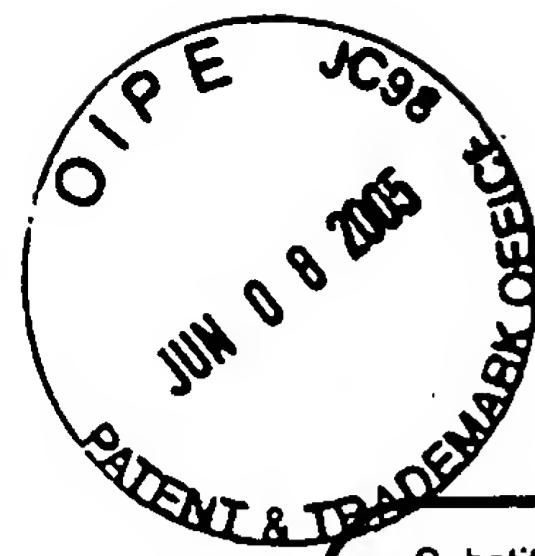
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	KB	MACKELLAR, C. et al., "Synthesis and physical properties of anti-HIV antisense oligonucleotides bearing terminal lipophilic groups," <i>Nucleic Acids Res.</i> (1992) 20(13): 3411-3417.	
	KC	MACMILLAN, A. et al, "Synthesis of Functionally Tethered Oligodeoxynucleotides by the Convertible Nucleoside Approach," <i>J. Org. Chem.</i> (1990) 55(24): 5931-5933.	
	KD	MANOHARAN, M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications," <i>Bioorganic Med. Chem. Letts.</i> (1994) 4(8): 1053-1060.	
	KE	MANOHARAN, M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents," <i>Nucleosides & Nucleotides</i> (1995) 14(3-5): 969-973.	
	KF	MANOHARAN, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides," <i>Antisense Strategies</i> , Baserga, R. and Denhardt, D. T. (eds.), The New York Academy of Sciences, New York, (1992) 660: 306-309.	
	KG	MANOHARAN, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications," <i>Bioorg. Med. Chem. Letts.</i> (1993) 3(12): 2765-2770.	
	KH	MANOHARAN, M. et al., "Lipidic Nucleic Acids," <i>Tetrahedron Letts.</i> (1995) 36(21): 3651-3654.	
	KI	MANOHARAN, M. et al., "Novel Functionalization of the Sugar Moiety of Nucleic Acids For Multiple Labeling in the Minor Groove," <i>Tetrahedron Letts.</i> (1991) 32(49): 7171-7174.	
	KJ	MARCUS-SEKURA, C. J., "Techniques for Using Antisense Oligodeoxyribonucleotides to Study Gene Expression," <i>Anal. Biochemistry</i> (1988) 172: 289-295.	
	KK	MARCUS-SEKURA, C. J. et al., "Comparative inhibition of chloramphenicol acetyltransferase gene expression by antisense oligonucleotide analogues having alkyl phosphotriester, methylphosphonate and phosphorothioate linkages," <i>Nucleic Acid Research</i> (1987) 15(14): 5749-5763.	
	KL	MARKIEWICZ, W. et al., "3',5'-O-(Tetraisopropylsiloxane-1,3-diyl)ribonucleosides," <i>Nucleic Acid Chemistry</i> Townsend, L. and Tipson, R. S. (eds.) J. Wiley and Sons, New York (1986): 229-231.	
	KM	MARKUSSEN, F.-H. et al., "Translational control of <i>oskar</i> generates a Short OSK, the isoform that induces pole plasm assembly," <i>Development</i> (1995) 121: 3723-3732.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 18 of 27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

NON PATENT LITERATURE DOCUMENTS

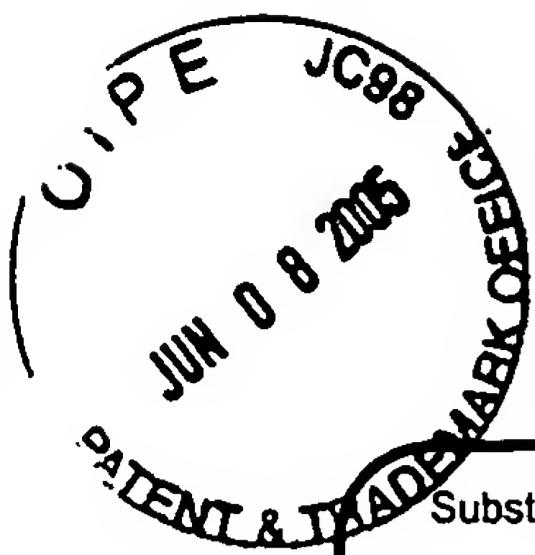
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	KN	MARLIN, S. D. et al., "A soluble form of intercellular adhesion molecule-1 inhibits rhinovirus infection," <i>Nature</i> (1990) 344: 70-72.	
	KO	MARTIN, P., "Ein newer Zugang zu 2'-O-Alkyribonucleosiden und Eigenschaften deren Oligonucleotide," <i>Helvetica Chemica Acta</i> (1995) 78: 486-504.	
	KP	MATSUKURA, M. et al., "Phosphorothioate analogs of oligodeoxynucleotides: Inhibitors of replication and cytopathic effects of human immunodeficiency virus," <i>Proc. Natl. Acad. Sci. USA</i> (1987) 84: 7706-7710.	
	KQ	MCDERMOTT, J. B. et al., "Structure and lens expression of the gene encoding chicken β A3/A1-crystallin," <i>Gene</i> (1992) 117: 193-200.	
	KR	MEYER, Jr., R. B. et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides," <i>J. Am. Chem. Soc.</i> (1989) 111(22):8517-9.	
	KS	MILLER, D. E. et al., "Cytokine modulation of intercellular adhesion molecule-1 surface expression of human melanoma cells; correlation with adhesion of peripheral blood leukocytes", <i>Proc. Am. Assoc. Cancer Res.</i> (1990) 31: 60, Abstract 353.	
	KT	MILLER, P. S. et al., "A new approach to chemotherapy based on molecular biology and nucleic acid chemistry: Matagen (masking tape for gene expression)," <i>Anti-Cancer Drug Des.</i> (1987) 2: 117-128.	
	KU	MILLER, P. S. et al., "Synthesis and Properties of Adenine and Thymine Nucleoside Alkyl Phosphotriesters, the Neutral Analogs of Dinucleoside Monophosphates," <i>J. Am. Chem. Soc.</i> (1971) 93(24): 6657-6665.	
	KV	MILLER, P. S. et al., "Nonionic Nucleic Acid Analogues. Synthesis and Characterization of Dideoxyribonucleoside Methylphosphonates," <i>Biochemistry</i> (1979) 18(23): 5134-5143.	
	KW	MILLER, P. S. et al., "Biochemical and Biological Effects of Nonionic Nucleic Acid Methylphosphonates," <i>Biochemistry</i> (1981) 20(7): 1874-1880.	
	KX	MIRABELLI, C. K. et al., "In vitro and in vivo pharmacologic activities of antisense oligonucleotides," <i>Anti-Cancer Drug Des.</i> (1991) 6: 647-661.	
	KY	MISHRA, R. K. et al., "Improved leishmanicidal effect of phosphorothioate antisense oligonucleotides by LDL-medicated delivery," <i>Biochim. et Biophysica</i> (1995) 1264: 229-237.	

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Sheet 19 of 27

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

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	KZ	MITCHELL, M. J. et al., "Boron trifluoride-methanol complex as a non-depurinating detritylating agent in DNA synthesis," <i>Nucleic Acids Res.</i> (1990) 18(17): 5321.	
	LA	MITSUNOBU, O., "The Use of Diethyl Azodicarboxylate and Triphenylphosphine in Synthesis and Transformation of Natural Products," <i>Synthesis</i> (1981): 1-28.	
	LB	MONACO, A. P. et al., "Studies on Heterologous Anti-Lymphocyte Serum in Mice", <i>J. Immunol.</i> (1966) 96(2): 229-238.	
	LC	MONACO, L. et al., "Structure of Two Rat Genes Coding for Closely Related Rolipram-sensitive cAMP Phosphodiesterases," <i>J. Biol. Chem.</i> (1994) 269(1): 347-357.	
	LD	MORI, K. et al., "Synthesis and Properties of Novel 5'-Linked Oligos," <i>Nucleosides & Nucleotides</i> (1989) 8(5&6): 649-657.	
	LE	MORICE, W. G. et al., "Rapamycin-induced Inhibition of p34 ^{cdc2} Kinase Activation is Associated with G ₁ /S-Phase Growth Arrest in T Lymphocytes," <i>J. Biol. Chem.</i> (1993) 268(5): 3734-3738.	
	LF	NAIR, V., "Development of Methodologies for the Strategic Modification of Purine Ribonucleoside Systems," <i>Nucleosides & Nucleotides</i> (1989) 8(5&6): 699-708.	
	LG	NELSON, P. S. et al., "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutants," <i>Nucleic Acids Res.</i> (1989) 17(18): 7187-7194.	
	LH	NICKOLOFF, B. J. et al., "Accessory Cell Function of Keratinocytes for Superantigens," <i>J. Immunol.</i> (1993) 150(6): 2148-2159.	
	LI	NIELSEN, P. E. et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide," <i>Science</i> (1991) 254: 1497-1500.	
	LJ	OBERHAUSER, B. et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol," <i>Nucleic Acids Res.</i> (1992) 20(3): 533-538.	
	LK	OHTSUKA, I. et al., "Recognition by restriction endonuclease <i>EcoRI</i> of deoxyoctanucleotides containing modified sugar moieties," <i>Eur. J. Biochem.</i> (1984) 139: 447-450.	
	LL	OKAYASU, I. et al., "A Novel Method in the Induction of Reliable Experimental Acute and Chronic Ulcerative Colitis in Mice," <i>Gastroenterology</i> (1990) 98: 694-702.	

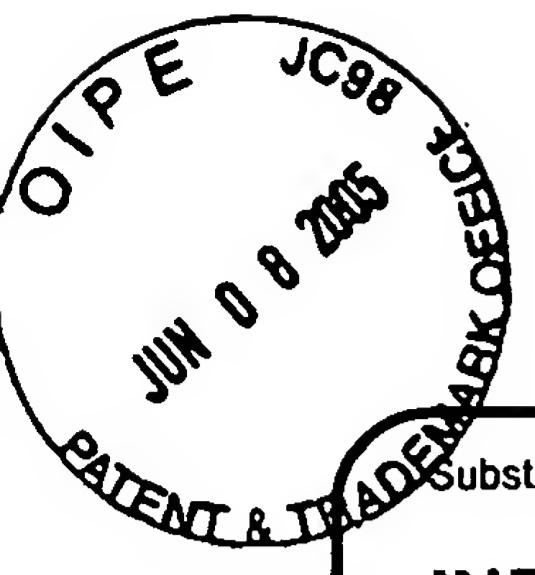
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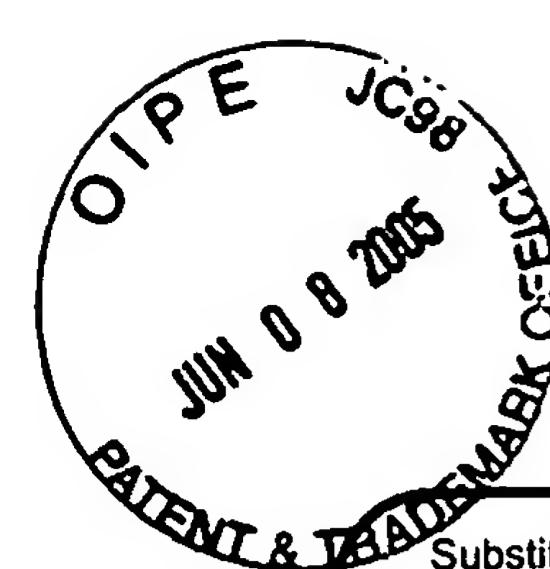
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	LM	OLSEN, S. R. et al., "Inhibition of Protein Kinase-A by Overexpression of the Cloned Human Protein Kinase Inhibitor," <i>Mol. Endocrinol.</i> (1991) 5: 1246-1256.		T ²
	LN	OSBORN, L. et al., "Direct Expression Cloning of Vascular Cell Adhesion Molecule 1, a Cytokine-Induced Endothelial Protein that Binds of Lymphocytes," <i>Cell</i> (1989) 59: 1203-1211.		
	LO	OUCHI, T. et al., "Synthesis and Antitumor Activity of Poly(Ethylene Glycol)s Linked to 5-Fluorouracil Via a Urethane or Urea Bond," <i>Drug Design and Discovery</i> (1992) 9: 93-105.		
	LP	OUTTEN, R. et al., "Synthetic 1-Methoxybenzo[d]naphtho[1,2- <i>b</i>]pyran-6-one C-Glycosides," <i>J. Org. Chem.</i> (1987) 52(22): 5064-5066.		
	LQ	PALFNER, K. et al., "Improvement of Hammerhead Ribozymes Cleaving <i>mdr-1</i> mRNA," <i>Biol. Chem. Hoppe-Seyler</i> (1995) 376: 289-295.		
	LR	PARKES, K. E. B. et al., "A Short Synthesis of 3'-Cyano-3'-Deoxythymidine", <i>Tetrahedron Letters</i> (1988) 29(24): 2995-2996.		
	LS	PERRI, S. et al., "Interactions of Plasmid-encoded Replication Initiation Proteins with the Origin of DNA Replication in the Broad Host Range Plasmid RK2," <i>J. Biol. Chem.</i> (1991) 266(19): 12536-12543.		
	LT	PETERSHEIM, M. et al., "Base-Stacking and Base-Pairing Contributions to Helix Stability: Thermodynamics of Double Helix Formation with CCGG, CCGGp, CCGGAp, ACCGGp, CCGGUp, and ACCGGUp," <i>Biochem.</i> (1983) 22(2): 256-263.		
	LU	PFITZNER, K. E. et al., "The Synthesis of Nucleoside-5' Aldehydes, " <i>J. Am. Chem. Soc.</i> (1963) 85: 3027.		
	LV	PIDGEON, C. et al., "Synthesis and Liposome Encapsulation of Antisense Oligonucleotide-Intercalator Conjugates, " <i>Annals New York Academy of Sciences</i> , 593-596.		
	LW	PUSHPA-REKA, T. R. et al., "Rat Phospholipid-hydroperoxide Glutathione Peroxidase," <i>J. Biol. Chem.</i> (1995) 270(45): 26993-26999.		
	LX	RAMIREZ, F. et al., "Nucleotidophospholipids: Oligonucleotide Derivatives with Membrane-Recognition Groups," <i>J. Am. Chem. Soc.</i> (1982) 104(20): 5483-5486.		
	LY	RANGANATHAN, R., "Modification of the 2'-Position of Purine Nucleosides: Synthesis of 2'- α -Substituted-2'-Deoxyadenosine Analogs," <i>Tetrahedron Letters</i> (1977) 15: 1291-1294.		

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 21 of 27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman
Attorney Docket Number	ISIS-5028

NON PATENT LITERATURE DOCUMENTS

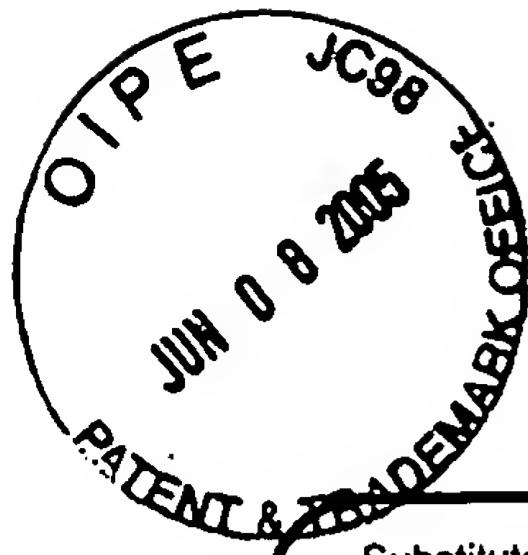
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	LZ	RAVASIO, N. et al., "Selective Hydrogenation Promoted by Copper Catalysts. 1. Chemoselectivity, Regioselectivity, and Stereoselectivity in the Hydrogenation of 3-Substituted Steroids," <i>J. Org. Chem.</i> (1991) 56(13): 4329-4333.	
	MA	REED, M. W. et al., "Acridine- and Cholesterol-Derivatized Solid Supports for Improved Synthesis of 3'-Modified Oligonucleotides," <i>Bioconjugate Chem.</i> (1991) 2(4): 217-225.	
	MB	REVANKAR, G. R. et al., "Synthesis and Antiviral/Antitumor of Certain 3-Deazaguanine Nucleosides and Nucleotides," <i>J. Med. Chem.</i> (1984) 27(11): 1389-1396.	
	MC	RICE, G. E. et al., "An Inducible Endothelial Cell Surface Glycoprotein Mediates Melanoma Adhesion," <i>Science</i> (1989) 246: 1303-1306.	
	MD	RICE, G. E. et al., "Inducible Cell Adhesion Molecule 110 (INCAM-110) is an Endothelial Receptor for Lymphocytes," <i>J. Exp. Med.</i> (1990) 171: 1369-1374.	
	ME	RICHERT, N. D. et al., "Stability and Covalent Modification of P-Glycoprotein in Multidrug-Resistant KB Cells," <i>Biochemistry</i> (1988) 27(20): 7607-7613.	
	MF	ROBINS, M. et al, "Nucleic Acid Related Compounds. 46. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides," <i>J. Am. Chem. Soc.</i> (1983) 105(12): 4059-4065.	
	MG	ROELEN, H. C. P. F. et al., "Synthesis of nucleic acid methylphosphonothioates," <i>Nucleic Acid Research</i> (1988) 16(15): 7633-7645.	
	MH	ROGERS, R. P. et al., "Alternative splicing dictates translational start in Epstein-Barr virus transcripts," <i>EMBO J.</i> (1990) 9(7): 2273-2277.	
	MI	RONINSON, I. B., "The Role of the MDR1 (P-Glycoprotein) Gene in Multidrug Resistance <i>In Vitro</i> and <i>In Vivo</i> ," <i>Biochem. Pharmacol.</i> (1992) 43(1): 95-102.	
	MJ	ROTHENBERG, M. et al., "Oligodeoxynucleotides as Anti-Sense Inhibitors of Gene Expression: Therapeutic Implications," <i>J. Natl. Cancer Inst.</i> (1989) 81(20): 1539-1544.	
	MK	RUBY, S. W. et al., "An Early Hierarchic Role of Ul Small Nuclear Ribonucleoprotein in Splicesome Assembly," <i>Science</i> (1988) 242: 1028-1035.	
	ML	SAISON-BEHMOARAS, T. et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," <i>EMBO J.</i> (1991) 10(5): 1111-1118.	

Examiner Signature	Date Considered
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 22 of 27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

NON PATENT LITERATURE DOCUMENTS

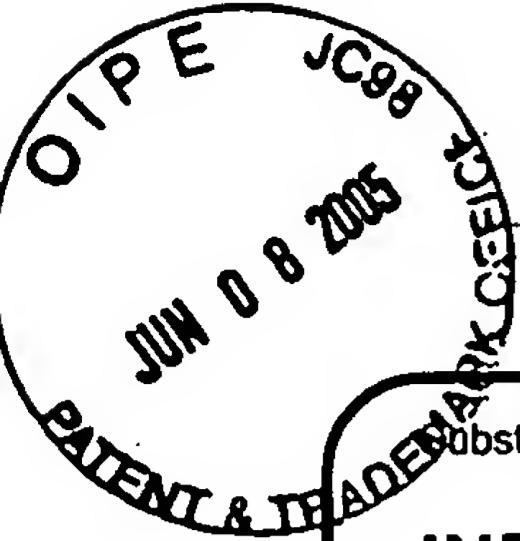
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	MM	SAMBROOK, J. et al. (eds.), "Preparation of Radiolabeled DNA and RNA Probes," <i>Molecular Cloning: A Laboratory Manual</i> (1989) 2d. Ed., p. 10.59.	
	MN	SAUL, D. J. et al., "celB, a Gene Coding for a Bifunctional Cellulase from the Extreme Thermophile " <i>Caldocellum saccharolyticum</i> ", " <i>Applied & Env. Microbiol.</i> (1990) 56: 3117-3124.	
	MO	SCANLON, K. J. et al., "Ribozyme-mediated reversal of the multidrug-resistant phenotype," <i>Proc. Natl. Acad. Sci. USA</i> (1994) 91: 11123-11127.	
	MP	SCHMIDT, R. R. et al., "C-Glycosides from O-Glycosyl Trichloroacetimidates," <i>Tetrahedron Letters</i> (1982) 23(4): 409-412.	
	MQ	SCHWARTZ, A. et al., "The DNA Bending by Acetylaminofluorene Residues and by Apurinic Sites," <i>J. Mol. Biol.</i> (1989) 207: 445-450.	
	MR	SEELA, F. et al., "Palindromic Octa- and Dodecanucleotides Containing 2'-Deoxytubercidin: Synthesis, Hairpin Formation, and Recognition by the Endodeoxyribonuclease EcoRI," <i>Biochemistry</i> (1987) 26(8): 2232-2238.	
	MS	SHEA, R. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates," <i>Nucleic Acids Res.</i> (1990) 18(13): 3777-3783.	
	MT	SHIBAHARA, S. et al., "Inhibition of human immunodeficiency virus (HIV-1) replication by synthetic oligo-RNA derivatives," <i>Nucleic Acids Research</i> (1987) 17(1): 239-252.	
	MU	SHIOHARA, T. et al., "Fixed Drug Eruption: Expression of Epidermal Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1)," <i>Arch. Dermatol.</i> (1989) 125: 1371-1376.	
	MV	SHOJI, Y. et al., "Mechanism of cellular uptake of modified oligodeoxynucleotides containing methylphosphonate linkages," <i>Nucleic Acids Res.</i> (1991) 19(20): 5543-5550.	
	MW	SIGMAN, D., "Nuclease Activity of 1,10-Phenanthroline-Copper Ion," <i>Acc. Chem. Res.</i> (1986) 19: 180-186.	
	MX	SIGMAN, D. S., "Chemical Nucleases," <i>Biochemistry</i> (1990) 29(39): 9097-9105.	
	MY	SIMONS, M. et al., "Antisense c-myb oligonucleotides inhibit intimal arterial smooth muscle cell accumulation <i>in vivo</i> ," <i>Nature</i> (1992) 359: 67-70.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 23 of 27

Complete if Known

Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman

Attorney Docket Number ISIS-5028

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	MZ	SINHA, N. D. et al., "The preparation and application of functionalized synthetic oligonucleotides: III. Use of H-phosphonate derivatives of protected amino-hexanol and mercapto-propanol or -hexanol," <i>Nucleic Acids Res.</i> (1988) 16(6): 2659-2669.	
	NA	SLUKA, J. et al., "Reagents and Methods for the Solid-Phase Synthesis of Protein-EDTA for Use in Affinity Cleaving," <i>J. Am. Chem. Soc.</i> (1990) 112(17): 6369-6374.	
	NB	SMITH, C. et al., "Antiviral effect of an oligonucleoside methylphosphonate) complementary to the splice junction of herpes simplex virus type 1 immediate early pre-mRNAs 4 and 5," <i>Proc. Natl. Acad. Sci. USA</i> (1986) 83: 2787-2791.	
	NC	SMITH-JONES, P. M. et al., "Antibody Labeling with Copper-67 Using the Bifunctional Macrocycle 4-[(1,4,8,11-Tetraazacyclotetradec-1-yl)methyl]benzoic Acid," <i>Bioconjugate Chem.</i> (1991) 2(6): 415-421.	
	ND	SOLOMONS, T. W. et al., <i>Organic Chemistry</i> (1980) John Wiley & Sons, New York, pp. 818-819.	
	NE	SPROAT, B. et al., "Highly efficient chemical synthesis of 2'-O-methyloligonucleotides and tetrabiotinylated derivatives; novel probes that are resistant to degradation by RNA or DNA specific nucleases," <i>Nucleic Acids Research</i> (1989) 17(9): 3373-3386.	
	NF	SPROAT, B. et al., "The synthesis of protected 5'-mercaptop-2', 5'-dideoxyribonucleoside-3'-O-phosphoramidites; uses of 5'-mercaptop-oligodeoxyribonucleotides," <i>Nucleic Acids Res.</i> (1987) 15(12): 4837-4848.	
	NG	SPROAT, B. S. et al., "New synthetic routes to protected purine 2'-O-methylriboside-3'-O-phosphoramidites using a novel alkylation procedure," <i>Nucleic Acids Research</i> (1990) 18: 41-49.	
	NH	STAUNTON, D. E. et al., "Primary Structure of ICAM-1 Demonstrates Interaction between Members of the Immunoglobulin and Integrin Supergene Families," <i>Cell</i> (1988) 52: 925-933.	
	NI	STAUNTON, D. E. et al., "A Cell Adhesion Molecule, ICAM-1, is the Major Surface Receptor for Rhinoviruses," <i>Cell</i> (1989) 56: 849-853.	
	NJ	STAUNTON, D. E. et al., "The Arrangement of the Immunoglobulin-like Domains of ICAM-1 and the Binding Sites for LFA-1 and Rhinovirus," <i>Cell</i> (1990) 61: 243-354.	
	NK	STEIN, C. et al., "Antisense Oligonucleotides as Therapeutic Agents-Is the Bullet Really Magical?" <i>Science</i> (1993) 261: 1004-1012.	
	NL	STEIN, C. A. et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review," <i>Cancer Research</i> (1988) 48: 2659-2668.	

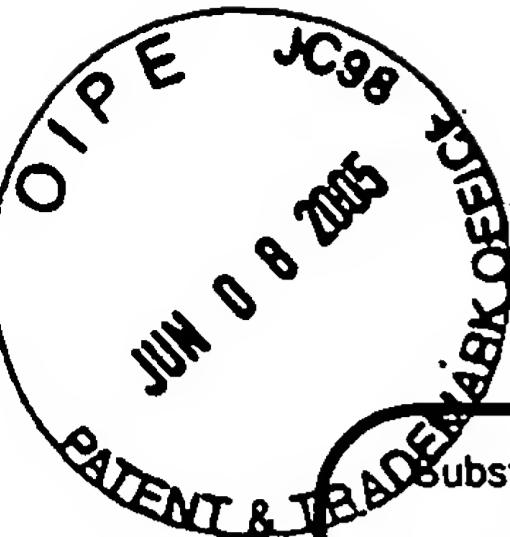
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Sheet

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman
Attorney Docket Number	ISIS-5028

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	NM	STEIN, C. A. et al., "Physicochemical properties of phosphorothioate oligodeoxynucleotides," <i>Nucleic Acids Research</i> (1988) 16(8): 3209-3221.	
	NN	STUFKENS, D. J., "Dynamic Jahn-Teller Effect in the Excited States of SeCl ₆ ²⁻ , SeBr ₆ ²⁻ , TeCl ₆ ²⁻ and TeBr ₆ ²⁻ ," <i>Recueil</i> (1970) 89: 1185-1201.	
	NO	SUCIU, N. et al., "Synthesis of 9-(2,5-dideoxy-β-D-glycero-pent-4-enofuranosyl)adenine," <i>Carbohydrate Res.</i> (1975) 44: 112-115.	
	NP	SVINARCHUK, F. P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," <i>Biochimie</i> (1993) 75: 49-54.	
	NQ	TELSER, J. et al., "Synthesis and Characterization of DNA Oligomers and Duplexes Containing Covalently Attached Molecular Labels: Comparison of Biotin, Fluorescin, and Pyrene Labels by Thermodynamic and Optical Spectroscopic Measurements," <i>J. Am Chem. Soc.</i> (1989) 111(18): 6966-6976.	
	NR	THIERRY, A. R. et al., "Overcoming multidrug resistance in human tumor cells using free and liposomally encapsulated antisense oligodeoxynucleotides," <i>Biochem. Biophys. Res. Comm.</i> (1993) 190(3): 952.-960	
	NS	TI, G. S. et al., "Transient Protection: Efficient One-Flask Synthesis of Protected Deoxynucleosides," <i>J. Am. Chem. Soc.</i> (1982) 104(5): 1316-1319.	
	NT	TIDD, D. M. et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues," <i>Anti-Cancer Drug Design</i> (1988) 3: 117-127.	
	NU	TSENG, B. et al., "Antisense oligonucleotide technology in the development of cancer therapeutics," <i>Cancer Gene Therapy</i> (1994) 1(1): 65-71.	
	NV	TWENTYMAN, P. R. et al., "A Comparison of Rhodamine 123 Accumulation and Efflux in Cells with P-Glycoprotein-mediated and MRP-associated Multidrug Resistance Phenotypes," <i>Eur. J. Cancer</i> (1994) 30A(9): 1360-1369.	
	NW	UESUGI, S. et al., "Improved Synthesis of 2'-Fluoro-2'-Deoxyadenosine and Synthesis and Carbon-13 NMR Spectrum of Its 3',5'-Cyclic Phosphate Derivative", <i>Nucleosides and Nucleotides</i> (1983) 2(4): 373-385.	
	NX	UESUGI, S. et al., "A Linear Relationship Between Electronegativity of 2'-Substituents and Conformation of Adenine Nucleosides," <i>Tetrahedron Letters</i> (1979) 42: 4073-4076.	

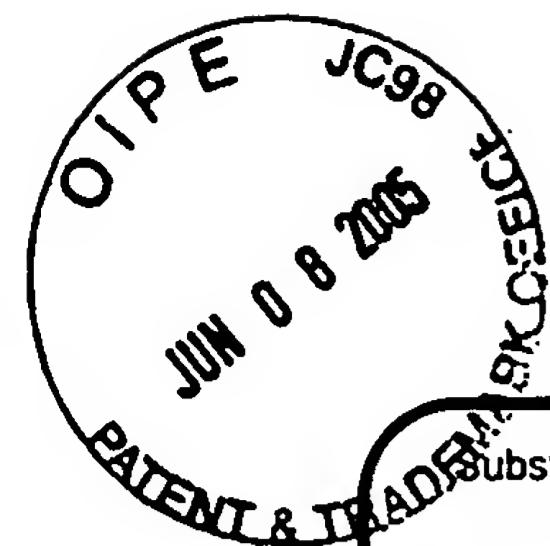
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Sheet

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Application Number	10/080,979
Filing Date	02/22/2002
First Named Inventor	Phillip Dan Cook
Art Unit	1635
Examiner Name	Amy Hudson Bowman
Attorney Docket Number	ISIS-5028

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	NY	UHLMANN, E. et al, "Antisense Oligonucleotides: A New Therapeutic Principle," <i>Chem. Rev.</i> (1990) 90(4): 543-584.	
	NZ	VAN DER KROL, A. R. et al., "Modulation of Eukaryotic Gene Expression by Complementary RNA or DNA Sequences," <i>BioTechniques</i> (1988) 6(10): 958-973.	
	OA	VASANTHAKUMAR, G. et al., "Modulation of Drug Resistance in Daunorubicin Resistant Subline with Oligonucleoside Methylphosphonates," <i>Cancer Comm.</i> (1989) 1(4): 225-232.	
	OB	VASSEUR, J.-J. et al., "Oligonucleosides: Synthesis of a Novel Methylhydroxylamine-Linked Nucleosides Dimer and its Incorporation into Antisense Sequences," <i>J. Am. Chem. Soc.</i> (1992) 114: 4006-4007.	
	OC	VEBER, D. et al., "Isonicotinyloxycarbonyl, a Novel Amino Protecting Group for Peptide Synthesis," <i>J. Org. Chem.</i> (1977) 42(20): 3286-3288.	
	OD	WAGNER, D. et al., "Preparation and Synthetic Utility of Some Organotin Derivatives of Nucleosides," <i>J. Org. Chem.</i> (1974) 39(1): 24-30.	
	OE	WALDER, J., "Antisense DNA and RNA: progress and prospects," <i>Genes Dev.</i> (1988) 2:502-4.	
	OF	WALDER, R. et al., "Role of RNase H in hybrid-arrested translation by antisense oligonucleotides," <i>Proc. Natl. Acad. Sci. USA</i> (1988) 85: 5011-5015.	
	OG	WEETMAN, A. P. et al., "Expression of an intercellular adhesion molecule, ICAM-1, by human thyroid cells," <i>J. Endocrinol.</i> (1989) 122: 185-191.	
	OH	WEGNER, C. D. et al., "Intercellular Adhesion Molecule-1 (ICAM-1) in the Pathogenesis of Asthma," <i>Science</i> (1990) 247: 456-459.	
	OI	WEISS, R., "Upping the Antisense Ante: Scientists bet on profits from reverse genetics," <i>Science News</i> (1991) 139: 108-109.	
*	OJ	WEISSBERGER, A. ed., <u>The Chemistry of Heterocyclic Compounds, Imidazole and Derivatives</u> , Interscience, N.Y., 1953.	
	OK	WELLICOME, S. M. et al., "A Monoclonal Antibody that Detects A Novel Antigen on Endothelial Cells is Induced by Tumor Necrosis Factor, IL-1, or Lipopolysaccharide", <i>J. Immunol</i> (1990) 144(7): 2558-2565.	

* A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.

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<i>Examiner Name</i>	Amy Hudson Bowman
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	OL	WESTERMANN, P. et al., "Inhibition of expression of SV40 virus large T-antigen by antisense oligodeoxyribonucleotides," <i>Biomed. Biochim. Acta</i> (1989) 48: 85-93.	
	OM	WU, T. et al., "Prevention of chain cleavage in the chemical synthesis of 2'-silylated oligoribonucleotides," <i>Nucleic Acids Res.</i> (1989) 17(9): 3501-3517.	
	ON	WYCHOWSKI, C. et al., "The Intranuclear Location of Simian Virus 40 Polypeptides VP2 and VP3 Depends on a Specific Amino Acid Sequence," <i>J. Virol.</i> (1987) 61(12): 3862-3869.	
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Examiner Signature

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 27 of 27

<i>Complete if Known</i>	
<i>Application Number</i>	10/080,979
<i>Filing Date</i>	02/22/2002
<i>First Named Inventor</i>	Phillip Dan Cook
<i>Art Unit</i>	1635
<i>Examiner Name</i>	Amy Hudson Bowman
<i>Attorney Docket Number</i>	ISIS-5028

NON PATENT LITERATURE DOCUMENTS

Examiner Signature		Date Considered	
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